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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/060,208	02/01/2002	Wilson Burgess	CI-0026	7581

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EXAMINER	
MCKANE, ELIZABETH L	
ART UNIT	**PAPER NUMBER**
1744	

DATE MAILED: 12/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/060,208	BURGESS ET AL.	
	Examiner	Art Unit	
	Leigh McKane	1744	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-123 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) 107 is/are allowed.

6)☒ Claim(s) 1-35,39-62,64,66-69,75,77-93,97,101-104 and 108-120 is/are rejected.

7)☒ Claim(s) 36-38,63,65,70-74,76,94-96,98-100,105,106 and 121-123 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5/27/03; 7/15/03; /12/02
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-4, 15-17, 19-26, 28-30, 34, 35, 39-41, 50-52, 54-62, 66-69, 75, 77, 78, 82-92, 102-104, 108-110, 112-118, and 120 are rejected under 35 U.S.C. 102(b) as being anticipated by Peterson (U.S. Patent No. 5,730,933).

Peterson teaches the use of e-beam or gamma radiation to sterilize a biological material (e.g. demineralized bone matrix) that is sensitive to radiation, wherein a stabilizer (antioxidant/free-radical scavenger, such as ascorbate or propyl galate) is added to the material prior to irradiation and the material is then irradiated within a package "under standard sterilization conditions...at an intensity and for a time duration sufficient to destroy substantially all of the microorganism contamination" (col.4, lines 59-64). See also col.4, lines 36-51; col.6, lines 1-18. The material may also be lyophilized or dried with drying agents and/or frozen and placed under a vacuum or inert gas, such as nitrogen or argon (col.4, lines 51-58; col.5, lines 28-35 and lines 53-67). The sterilized tissue may be used to treat a disease or deficiency and retains about 50% to about 100% of its initial biological activity. See col.3, lines 3-7 and col.6, lines 29-32.

3. Claims 1-4, 10-14, 28, 39, 42, 49, 54, 55, 64, 77, 79, 80-88, 93, 97, 101, 102, 104, 108-110, and 112-120 are rejected under 35 U.S.C. 102(b) as being anticipated by Odland (U.S. Patent No. 5,989,498).

Odland teaches the sterilization of sensitive biological materials (packaged heart valves) at ambient temperature to slightly above ambient (col.4, lines 35-37 and 48-51) with e-beam radiation. Prior to radiation, the biological material is stabilized (cross-linked) with a stabilizer mixture (cross-linking agents) and immersed in a non-aqueous solvent (ethanol) to reduce calcification. See col.7, lines 38-58. The material is then irradiated with e-beam radiation at a dose rate of 2.2×10^4 kGy/hr (col.3, line 24). The sterilized material may be used to treat a human. See col.1, lines 14-23. Moreover, Odland discloses that e-beam sterilization does not have a negative effect on durability of heart valves and in fact, when combined with cross-linking improves durability. See Example 6.

4. Claims 1, 27, 43-45, and 53 are rejected under 35 U.S.C. 102(b) as being anticipated by Horowitz et al (U.S. Patent No. 5,712,086).

Horowitz et al teaches a method of radiation sterilizing sensitive biological materials combined with stabilizer mixtures and sensitizers. See Abstract. The stabilizer can be glutathione or vitamins, among others. The biological material may be immunoglobulins (col.5, lines 66-67). Horowitz et al discloses exposing the materials to particular fluences of radiation (col6, lines 57-62) for particular time periods (col.7, lines 45-48) and at temperatures slightly above ambient (col.6, lines 41-43). Radiation sources include UV, gamma, x-rays, and visible light.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 5, 27, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peterson in view of Horowitz et al.

As to claim 5, although Peterson fails to teach removal of an organic solvent from the biological material, Horowitz et al discloses that it was known in the art to combine the treatment

of a biological material with irradiation and a stabilizer mixture with a second virucidal treatment such as, treatment with an organic (lipid) solvent. See col.7, line 66 to col.8, line 8. As such merely improves the virucidal effectiveness of the method of Peterson it would have been obvious to first treat the biological material with the organic solvent, followed by removal prior to irradiation.

With respect to claims 27 and 31, Peterson does not teach adding a sensitizer to the material prior to irradiation or a combination stabilizer. Horowitz et al, however, teaches a method of sterilizing sensitive biological materials wherein a sensitizer and a stabilizer mixture is preferably added prior to irradiation. See Abstract; col.3, lines 34-39, lines 45-47, lines 60-62. As the sensitizer combined with radiation is disclosed to kill viruses without undue damage to the valuable biological material, it would have been an obvious addition to the method of Peterson. Moreover, since Horowitz et al teaches that a combination stabilizer quenches both free radicals and reactive forms of oxygen and thus, achieves preferential damage to the virus, it would have been obvious to use such in the method of Peterson.

9. Claims 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peterson in view of Kent (U.S. Patent No. 6,171,549).

Peterson teaches irradiation "under standard sterilization conditions...at an intensity and for a time duration sufficient to destroy substantially all of the microorganism contamination" (col.4, lines 59-64). Peterson does not specify what the intensity (dose rate) is. Kent, however, teaches that when sterilizing sensitive biological materials with gamma radiation, one should choose a low dose rate (0.1-3.0 kGy/hr). See Abstract. As this dose rate is disclosed by Kent to be effective in sterilizing without undue damage to the biological material, it would have been

obvious to use in Peterson.

10. Claims 18 and 111 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peterson.

Peterson teaches subjecting the biological material to a vacuum or inert gaseous atmosphere prior to irradiation in order to remove oxygen. However, it is deemed obvious to do both in combination any number of time necessary to assure that all oxygen has been removed from the material.

11. Claims 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peterson in view of Stieglitz (DE 3817603).

Peterson fails to disclose stabilizing the biological material with heparin. However, Stieglitz teaches that when sterilizing blood, it is necessary to add heparin thereto in order to avoid clotting. As Peterson teaches that the biological material may be blood, one would have found it obvious to add heparin when the material is blood.

12. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Odland in view of Horowitz et al.

Odland does not teach adding a sensitizer to the material prior to irradiation. Horowitz et al, however, teaches a method of sterilizing sensitive biological materials wherein a sensitizer and a stabilizer mixture is preferably added prior to irradiation. See Abstract; col.3, lines 34-39, lines 45-47, lines 60-62. As the sensitizer combined with radiation is disclosed to kill viruses without undue damage to the valuable biological material, it would have been an obvious addition to the method of Odland.

13. Claims 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horowitz et al.

Although Horowitz et al does not specifically teach the use of polychromatic visible light, infrared, or a combination of visible and UV radiation, it is disclosed that the "term "irradiation" is to be construed broadly to include any form of radiation conventionally used to inactivate cells...either alone or combined with some other agent or condition." See col.6, lines 48-53. Thus, it is deemed obvious to use other known forms of radiation in the method of Horowitz et al.

Allowable Subject Matter

14. Claims 36-38, 63, 65, 70-74, 76, 94-96, 98-100, 105, 106, and 121-123 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

15. Claim 107 is allowed.

16. The following is a statement of reasons for the indication of allowable subject matter: the prior art of record fails to teach or suggest: the claimed stabilizer mixtures; a dipeptide stabilizer; a glassy or vitrified biological material; PPG or DMSO as the non-aqueous solvent; a residual solvent content of 7, 9, 10, 20, or 33%; the use of a compound effective to increase penetration of the stabilizer; or an assay for determining the optimal conditions for sterilizing a collagen containing tissue.

Claim Objections

17. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 121 and 122 have been renumbered 122 and 123.

Conclusion

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh McKane whose telephone number is 703-305-3387 until December 15, 2003. After December 15, 2003 the examiner can be reached at 571-272-1275. The examiner can normally be reached on Monday-Wednesday (7:15 am-4:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert J. Warden can be reached on 703-308-2920 or at 571-272-1281 after December 15, 2003. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0661.

Leigh McKane

Leigh McKane
Primary Examiner
Art Unit 1744

elm
1 December 2003